

LEGAL ASPECTS OF ANIMAL-HUMAN COMBINATIONS IN CANADA

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This article examines the current legal regime applicable to animal-human combinations under the Assisted Human Reproduction Act (Canada). The Act prohibits as criminal offences the use of non-human reproductive material in humans, the use in humans of human reproductive material previously transplanted into a non-human life form, the creation of chimeras made from human embryos, and the creation for reproductive purposes of human/non-human hybrids. Additional animal-human combinations, such as transgenic life forms, may be regulated pursuant to section 11 of the Act in the future.

The underlying concerns of the Act in establishing this regime appear to be the protection of human health and safety, human dignity and individuality, and the human genome. The Act seems calibrated to prohibit the creation of animal-human combinations that are currently unsafe and scientifically and ethically problematic, while leaving open the possibility of regulating other such combinations with more immediate scientific potential, although these also raise ethical questions.

Currently, certain differences subsist in Canada between what is permissible for researchers and institutions funded by federal agencies and those in privately funded research. The development of the regulatory framework under the Act will reveal how freedom of research will be balanced against the need for scientifically valid and ethically justifiable research, and whether these differences will continue to apply.

INTRODUCTION	84
I. HISTORICAL BACKGROUND AND STRUCTURE OF THE <i>AHRA</i>	84
A. Purpose and Overview of the <i>AHRA</i> ; Declaration	85
B. Prohibitions Relating to Animal-Human Combinations	86
C. Controlled Activities	89
II. CHIMERAS AND HYBRIDS IN THE <i>AHRA</i> AND THE CIHR RESEARCH GUIDELINES	90
III. ENFORCEMENT: OFFENCES AND GRANDFATHERING CLAUSE	92
IV. CONSTITUTIONAL NOTE	93
V. ETHICAL CONSIDERATIONS UNDERLYING THE REGULATION OF ANIMAL-HUMAN COMBINATIONS IN THE <i>AHRA</i>	94
A. Health and Safety	94
B. Human Dignity	95
C. Individuality	98
D. Protection of the Human Genome	98
CONCLUSION	99

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INTRODUCTION

Recent press coverage underlines the fact that we are moving towards a world that was science fiction not so long ago: mice and chimpanzees with partly human brains now inhabit our laboratories;¹ pigs with human lymphocytes are being designed as possible sources of organs for transplantation into humans;² and rabbit oocytes have been fused with human cells to make hybrid embryos.³ These developments have raised ethical and legal questions, and have led to calls for regulation, although the question of what constitutes appropriate regulation is not easily resolved. Recently, the British Human Embryology and Fertilisation Authority made news when it decided to postpone a decision to license experiments involving nuclear transfer of a human somatic cell into animal eggs until a public consultation process is completed.⁴

As noted by Henry Greely, there are many possible types of interspecies mixtures.⁵ Providing examples of both naturally occurring and artificial combinations, he proposed a taxonomy of these based on several criteria—the type of biological material combined, the relevant species included in the combination, and the developmental stage at which the combination is performed, for example. The mule is an example of a naturally occurring interspecies mixture known to man for millennia.⁶ In contrast, the transplantation of animal organs into human beings, such as a baboon heart in a human child, is a recent development that has not been entirely successful.⁷

In 2004, Canada passed the *Assisted Human Reproduction Act* (*AHRA* or the *Act*), which also addresses some types of animal-human combinations at the genetic, cellular, and tissue levels.⁸ This paper will briefly review the current legislative framework dealing with animal-human combinations in this statute and consider the ethical themes underpinning it. After some background information concerning the passage and structure of the *Act*, the regulatory scheme it proposes concerning animal-human combinations will be described, as will some of the differences between the legislative scheme contained in the *AHRA* and the currently applicable federal guidelines for research funding. A brief overview of the relevant ethical considerations explicitly referred to in the *Act* will then be undertaken, with reference to some international instruments.

Although man is “*un animal doué de raison*”,⁹ the reader should be aware that for simplicity the term “animal” is used throughout this paper as meaning “non-human animal”.

I

HISTORICAL BACKGROUND AND STRUCTURE OF THE *AHRA*

The process of adopting legislation concerning assisted human reproduction was long and protracted in Canada, and is discussed here with an emphasis on animal-human combinations. A Royal Commission on New Reproductive Technologies was appointed in 1989 and produced its final report in 1993. This final

¹ Irving Weissman at Stanford University is working on mice with brains that contain human neurons; reported in, among others, Sharon Begley, “Science Journal: Chimeras exist, and what if some turn out to be too human?” *The Wall Street Journal* (6 May 2005), online: The Pittsburgh Post-Gazette <<http://www.post-gazette.com/pg/05126/500265.stm>>. Experiments with African green monkeys receiving human neurons are taking place at the St. Kitts Biomedical Research Foundation: see Tim Bearden, “Chimeras: Animal-Human Hybrids” *Online News Hour PBS* (16 August 2005), online: Public Broadcasting Service Online News Hour <http://www.pbs.org/newshour/bb/science/july-dec05/chimera_8-16.html>.

² At the Mayo Clinic in Rochester, Minnesota, Christopher McGregor is working on designing such pigs. See Mayo Clinic, News Release, “Mayo Investigator Awarded \$4.5 Million from NIH for Transplant Research” (11 July 2005), online: Mayo Clinic <<http://www.mayoclinic.org/news2005-rst/2930.html>>.

³ See, among others, Maryann Mott, “Animal-Human Hybrids Spark Controversy” *National Geographic News* (25 January 2005), online: National Geographic <http://news.nationalgeographic.com/news/2005/01/0125_050125_chimeras.html>.

⁴ Human Fertilisation and Embryology Authority, News Release, “Press Statement Regarding Human-Animal Hybrid Research” (11 January 2007), online: Human Fertilisation and Embryology Authority <<http://www.hfea.gov.uk/cps/rde/xchg/SID-3F57D79B-C3CE7A8F/hfea/hs.xsl/1478.html>> [HFEA Press Statement].

⁵ Henry T. Greely, “Defining Chimeras... and Chimeric Concerns” (2003) 3:3 *American Journal of Bioethics* 17.

⁶ Mules, generically, are the result of a cross between a female horse and a male donkey.

⁷ Lawrence K. Altman, “Baboon’s heart implanted in infant on coast” *The New York Times* (28 October 1984), online: The New York Times <<http://query.nytimes.com/gst/fullpage.html?sec=health&res=9C01E1DD1239F93BA15753C1A962948260>>.

⁸ S.C. 2004, c. 2 [*AHRA*].

⁹ Robert Merle, *Un animal doué de raison* (Paris: Gallimard, 1967).

report recommended that the creation of animal-human hybrids be criminally prohibited.¹⁰ In July of 1995, the federal government called a voluntary moratorium on nine reproductive technologies, including the creation of animal-human hybrids.

In 1996, Bill C-47¹¹ was tabled; its goal was the criminal prohibition of certain practices, including the fertilization of human ova by animal sperm (or the converse manipulation) for the purpose of producing a zygote capable of differentiation; the fusion of human and animal zygotes or embryos; and the implantation of a human embryo in an animal, or of an animal embryo in a woman. At the same time, a document entitled *New Reproductive Technologies: Setting Boundaries, Enhancing Health*¹² was tabled to propose a framework for the regulation of those reproductive technologies that were not prohibited, and thus achieve an integrated approach to reproductive technologies. The proposed framework did not deal with animal-human combinations specifically.

Bill C-47 was never passed, and in 2001 Health Canada issued the *Proposals for Legislation Governing Assisted Human Reproduction*¹³ for review by the House of Commons Standing Committee on Health. The *Proposals* would have prohibited the transplantation of animal reproductive material into a human and the use of human reproductive material previously transplanted into an animal. The creation of both chimeras and transgenic animals was to be regulated under a licensing system.

The Standing Committee on Health's response emphasized the necessity of forbidding the creation and use of all animal-human hybrids for the purpose of reproduction, in addition to the proposed prohibitions.¹⁴ No recommendation was made with respect to the animal-human combinations subject to a licensing regime.

Bill C-56, which reflected the recommendations of the Standing Committee, was tabled in May of 2002;¹⁵ it was not passed during this session and was resubmitted twice, first as Bill C-13¹⁶ in October of 2002 and then as Bill C-6¹⁷ in January of 2004. Finally, more than a decade after the publication of the Royal Commission's final report, the AHRA received royal assent on March 29, 2004.¹⁸

A. Purpose and Overview of the AHRA; Declaration

The purpose of the AHRA is to regulate assisted human reproductive technologies and related research, and to secure their benefits for individuals, families, and society.¹⁹ Certain types of animal-human combinations can be created by using reproductive materials and techniques, which explains why they are dealt with in this statute.

The Act prohibits certain activities (such as reproductive or research cloning or the knowing creation of transmissible mutations in a person's genome)²⁰ and regulates others through a licensing scheme (such as the use of human reproductive material to create an embryo).²¹ An agency with licensing and enforcement powers, the Assisted Human Reproduction Agency of Canada (the Agency), is created to administer the Act.²² A special regime of privacy and access to personal information collected pursuant to

¹⁰ Canada, *Proceed with Care—Final Report of the Royal Commission on New Reproductive Technologies*, vol. 1 (Ottawa: Canada Communications Group, 1993) at 636–637 [Commission Report].

¹¹ *An Act respecting human reproductive technologies and commercial transactions relating to human reproduction*, 2nd Sess., 35th Parl., 1996.

¹² Canada, Health Canada, *New Reproductive and Genetic Technologies: Setting Boundaries, Enhancing Health* (Ottawa: Minister of Supplies and Services, 1996).

¹³ Health Canada, *Proposals for Legislation Governing Assisted Human Reproduction*, (Draft 2001), online: Health Canada <http://www.hc-sc.gc.ca/ahc-asc/alt_formats/cmcd-dcmc/pdf/media/releases-communiques/2001/legislation.pdf> [Proposals].

¹⁴ House of Commons, Standing Committee on Health, *Assisted Human Reproduction: Building Families*, December 2001, online: Standing Committee on Health <<http://cmte.parl.gc.ca/cmte/CommitteePublication.aspx?COM=218&Lang=1&SourceId=37082>>, recommendation 8 [Standing Committee Report].

¹⁵ Bill C-56, *An Act respecting human reproduction*, 1st Sess., 37th Parl., 2002.

¹⁶ Bill C-13, *An Act respecting human reproduction*, 2nd Sess., 37th Parl., 2002.

¹⁷ Bill C-6, *An Act respecting human reproduction*, 3rd Sess., 37th Parl., 2004.

¹⁸ The AHRA was proclaimed into force on April 22, 2004 except for ss. 8, 12, 14 to 19, 21 to 59, 72 and 74 to 77, S.I./2004-49, C. Gaz. 2004.II.478. Sections 21 to 39, 72, 74, 75 and 77 of the AHRA came into force January 12, 2006, except for paragraphs 24(1)(a), (e) and (g), S.I./2005-42, C.Gaz. 2005.II.1033.

¹⁹ AHRA, *supra* note 8, s. 2(b).

²⁰ *Ibid.*, ss. 5–9 (all currently in force).

²¹ *Ibid.*, ss. 10–13 (s. 12 is not currently in force).

²² *Ibid.*, ss. 21–39.

the *Act* is provided for.²³ Offences are created,²⁴ and provision is made for the enactment of regulations.²⁵ The administration of the *AHRA* will be reviewed within three years of the creation of the Agency by a committee of the legislature, which will provide recommendations for changes to the *AHRA* or its administration.²⁶

Important portions of the *AHRA* have still not been proclaimed into force.²⁷ Some that are technically in force have no practical effect; for instance, although the provisions creating the Agency came into force on January 12, 2006, the Agency is not operational at the time of the writing of this article, although in December of 2006, a President, Chairperson, and Board of Directors were named.²⁸ Those sections that depend on the existence of regulations to have any effect²⁹ provide another illustration of this, because no regulations have been enacted. As a result, the only currently operative portions of the *AHRA*, in addition to the interpretive provisions, are those setting out prohibited activities and the sanctions attached to contraventions of these prohibitions. Although public consultations have begun on some aspects of regulation under the *AHRA*,³⁰ to date these consultations have not resulted in any further governmental action.

B. Prohibitions Relating to Animal-Human Combinations

The *AHRA* prohibits the following activities with respect to animal-human combinations:³¹

(i) *transplantation of a sperm, ovum, embryo or foetus of a non-human life form into a human being.*³²

The terms “sperm”, “ovum”, “embryo”, and “foetus” are all defined with reference to human beings in the *AHRA*, but the context of this provision clearly requires that the definitions not be referred to for its interpretation.

This prohibition seems to be aimed principally at the possible creation of a being containing mixed genetic or reproductive material from human and non-human species, and at the possibility of a human being acting as surrogate for a non-human life form.

(ii) *for the purpose of creating a human being, make use of any human reproductive material or an in vitro embryo that is or was transplanted into a non-human life form.*³³

“Human reproductive material” is defined as “a sperm, ovum or other human cell or a human gene, and includes a part of any of them.”³⁴ It is not limited to germ line cells but includes a somatic cell that

²³ *Ibid.*, ss. 14–19 (none is currently in force).

²⁴ *Ibid.*, ss. 60–64.

²⁵ *Ibid.*, ss. 65–67.

²⁶ *Ibid.*, s. 70.

²⁷ These include provisions dealing with the use of reproductive material without consent, reimbursement of surrogate mothers' expenses, the privacy and access to information regime, and sections dealing with the operation of the Agency; the sections creating the Agency came into force on January 12, 2006.

²⁸ Health Canada, News Release, “Canada’s New Government announces a President, Chairperson and Board of Directors for Assisted Human Reproduction Canada” (21 December 2006), online: Health Canada <http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/2006/2006_133_e.html>.

²⁹ For instance, most controlled activities require a licence delivered in accordance with the regulations, but no regulations have been adopted concerning the licensing conditions. A similar situation occurs with section 11 of the *AHRA*, apparently aimed at the creation of transgenics, which requires a licence for certain types of interspecies combinations at the genetic level, with the particulars to be provided by regulation (see section I(C) below).

³⁰ Health Canada gave notice in October of 2004 that it intended to develop the components of the regulatory framework under the *AHRA* and announced its intention to undertake public involvement activities for the development of these components (C. Gaz. 2004.I.3003). This process was initiated for section 8 (Consent) of the *AHRA* and draft regulations were published in September of 2005 (C. Gaz. 2005.I.3165). Workshops have been held on several topics, such as expense reimbursement for gamete donors and counselling for reproductive services; public comment has been requested on preimplantation genetic diagnosis, for example, and a public consultation is currently ongoing for counselling services. None of these activities has been concerned with animal-human combinations, however.

³¹ *AHRA*, *supra* note 8, s. 5(1). The introductory language of this provision states that “no person shall knowingly ...”, so knowledge of what one is doing is necessary for these prohibitions to apply.

³² *Ibid.*, s. 5(1)(g).

³³ *Ibid.*, s. 5(1)(h).

might be used for cloning by nuclear transfer,³⁵ for example. Thus, the intention is clearly that the *Act* cover methods of reproduction beyond fertilization. “Sperm” and “ovum” are also defined in the *AHRA* and refer in each case to the human sperm or ovum, whether mature or not. As noted by others, the reference to maturity in these definitions will prevent the use of earlier-stage gametes to circumvent the prohibitions or controls provided for in the *Act*.³⁶

“Embryo” is defined as “a human organism during the first 56 days of its development following fertilization or creation, excluding any time during which its development has been suspended, and includes any cell derived from such an organism that is used for the purpose of creating a human being.”³⁷ Here also, the intent to cover methods of reproduction other than fertilization is clear from the use of the word “creation”. Presumably, this language was inspired by the desire to avoid a situation like the *Quintavalle*³⁸ case in the United Kingdom, which dealt with the interpretation of the term “embryo” in the British *Human Fertilisation and Embryology Act 1990*.³⁹ The House of Lords confirmed the Court of Appeal’s decision that the word “embryo”, although defined in the British *Act* solely by reference to fertilization, should be interpreted to include the result of nuclear transfer.

Since the prohibition applies only “for the purpose of creating a human being”, the use of human reproductive material previously transplanted into an animal for cell or gene therapy is not covered here. Thus, the use of xenotransplants from animals modified to carry human genes, for example, would not be prohibited by this section. However, the use of animal surrogates for human beings is clearly prohibited.

(iii) create a chimera, or transplant a chimera into either a human being or a non-human life form.⁴⁰

A “chimera” is defined as either

- (a) an embryo into which a cell of any non-human life form has been introduced; or
- (b) an embryo that consists of cells of more than one embryo, foetus or human being.⁴¹

Two remarks should be made here: firstly, the prohibition applies only at the embryonic stage, so that cell therapy (or the introduction of “foreign” cells for other purposes), and tissue and organ transplants (from human or animal sources) at fetal or later developmental stages are not prohibited. Secondly, because embryos are defined as human embryos in the *Act*, only animal-to-human⁴² chimeras or human-to-human chimeras are prohibited. Human-to-animal⁴³ combinations such as introducing human cells into embryonic animals are not targeted by this provision.

A recent search revealed no reported experiments involving the creation of “chimeras”, as defined in the *AHRA*, in the current scientific literature, although experiments involving the introduction of animal brain cells into *adult* humans suffering from Parkinson’s disease, for example, have been carried out.⁴⁴ However, experiments involving the introduction of human cells into animal embryos (the converse of a chimera, as described in the *AHRA*) are performed in various contexts.⁴⁵ These experiments variously attempt to test the capacity and mechanisms of differentiation of human cells during development, to

³⁴ *AHRA*, *supra* note 8, s. 3.

³⁵ Nuclear transfer, the process used to clone the famous sheep Dolly, involves using an oocyte (egg cell) from which the nucleus has been removed, and introducing the nucleus of a cell from the organism to be cloned into the egg. After appropriate stimulation, the egg with the new nucleus can be induced to divide and develop as an embryo and, sometimes, into an adult animal. For an interesting historical and technical account of the cloning of Dolly the sheep, see Ian Wilmut & Roger Highfield, *After Dolly—The Uses and Misuses of Human Cloning* (New York: W. W. Norton Company Inc., 2006).

³⁶ Glenn Rivard & Judy Hunter, *The Law of Assisted Human Reproduction* (Markham: LexisNexis/Butterworths, 2005) at 44.

³⁷ *AHRA*, *supra* note 8, s. 3.

³⁸ *R (Quintavalle) v. Secretary of State for Health*, 2003 UKHL 13, [2003] 2 A.C. 687 (H.L.) [*Quintavalle*].

³⁹ (U.K.), 1990, c. 37.

⁴⁰ *AHRA*, *supra* note 8, s. 5(1)(i).

⁴¹ *Ibid.*, s. 3.

⁴² Meaning chimeras created by adding animal cells to a human embryo.

⁴³ Meaning chimeras created by adding human cells to an animal embryo.

⁴⁴ J. Stephen Fink *et al.*, “Porcine xenografts in Parkinson’s disease and Huntington’s disease patients: preliminary results” (2000) 9 *Cell Transplant* 273.

⁴⁵ Alysson R. Muotri *et al.*, “Development of functional human embryonic stem cell-derived neurons in mouse brain” (2005) 102:51 *Proceedings of the National Academy of Science of the USA* 18644.

create models for the study of certain types of disease, and to develop better sources of cells for transplantation into humans.

One author, Baylis, questions whether the prohibition in the *AHRA* is too narrow,⁴⁶ and contrasts the *Act* with the stem cell research guidelines adopted by the Canadian Institutes of Health Research (CIHR). These guidelines proscribe a greater range of chimera-making, including the introduction of human pluripotent cells into animal embryos.⁴⁷ The differences between the *AHRA* and the *Stem Cell Guidelines* are further discussed in section II below, and arise as a result of the divergent goals of these instruments. Baylis also supposes that those chimeras not prohibited by section 5 of the *Act* might be regulated under section 11,⁴⁸ which is discussed in section I(C) below.

Both the creation and the transplantation of a chimera into any life form are prohibited by the *Act*; thus, no pre-transplantation experimentation may take place with chimeras, whereas the situation appears to be different for hybrids.

*(iv) create a hybrid for the purpose of reproduction, or transplant a hybrid into either a human being or a non-human life form.*⁴⁹

A “hybrid” is defined as

- (a) a human ovum that has been fertilized by a sperm of a non-human life form;
- (b) an ovum of a non-human life form that has been fertilized by a human sperm;
- (c) a human ovum into which the nucleus of a cell of a non-human life form has been introduced;
- (d) an ovum of a non-human life form into which the nucleus of a human cell has been introduced; or
- (e) a human ovum or an ovum of a non-human life form that otherwise contains haploid sets of chromosomes from both a human being and a non-human life form.⁵⁰

This prohibition is aimed only at the creation of hybrids for reproductive purposes and at their transplantation into a life form, which would permit further development and, eventually, birth. The possibility remains that hybrids could be created *in vitro* for purposes of research, for example, and that development might take place *in vitro* for some time, as long as the purpose of the experiment is not “reproductive”.⁵¹ This does raise the question of how far such development might be allowed to take place, but the *AHRA* does not address this directly; regulations may do so in the future. This question is not academic, as experiments have been carried out in which human nuclei have been transferred into rabbit oocytes⁵² to create what would qualify as “hybrid” embryos in an attempt to generate human embryonic stem cells for research. This technique would have the advantage of producing essentially human⁵³ embryonic stem cells for research purposes without making use of human eggs, a scarce and ethically problematic resource. These hybrid embryos could also prove a useful tool for the study of the reprogramming and differentiation of human nuclei.

Here also, the *Act* attempts to anticipate potential technological developments: the final clause of the definition of hybrids considers their creation by any method that leads to the creation of a human or non-

⁴⁶ Françoise Baylis, “Betwixt and Between Human Stem Cell Guidelines and Legislation” (2002) 11:1 Health Law Review 44.

⁴⁷ Canadian Institutes of Health Research, *Updated Guidelines for Human Pluripotent Stem Cell Research*, June 28, 2006, online: Canadian Institutes of Health Research <<http://www.cihr-irsc.gc.ca/e/31488.html>> [*Stem Cell Guidelines*].

⁴⁸ *Supra* note 46.

⁴⁹ *AHRA*, *supra* note 8, s. 5(1)(j).

⁵⁰ *Ibid.*, s. 3.

⁵¹ This also means that certain techniques used to test the suitability of sperm for fertilization, such as the incubation of human sperm with hamster oocytes, will not be prohibited.

⁵² Chen Ying *et al.*, “Embryonic stem cells generated by nuclear transfer of human somatic nuclei into rabbit oocytes” (2003) 13:4 Cell Research 251. For a recent report of interspecies nuclear transfer (mouse nuclei transferred into cow oocytes), see Gretchen Vogel, “Team Claims Success With Cow-Mouse Nuclear Transfer” (2006) 313 Science 155.

⁵³ During nuclear transfer to produce such a hybrid embryo, the nucleus of a human cell would be introduced in an animal egg from which the nucleus has been removed, as described in note 35, *supra*. Most of the genetic material in a cell is located in the nucleus; therefore the resulting embryo would be “mostly” human. Animals’ cells also contain small organelles known as mitochondria, which are involved in generating energy; these mitochondria would remain present in the hybrid embryo, and contain some genes coding for proteins involved in energy metabolism. The “hybrid embryo” would therefore also contain a very small number of animal genes (37) in addition to all the human nuclear genes (currently estimated at approximately 23,000 genes). See Human Genome Project Information, *How many genes are in the human genome?*, online: <http://www.ornl.gov/sci/techresources/Human_Genome/faq/genenumber.shtml>.

human ovum with haploid sets of chromosomes from both a human and non-human life form. It does not seem to catch the situation in which a cell other than an ovum is used as starting material for the creation of such an organism, something which is not currently technically possible but which might become so. However, section 11 of the *AHRA*, discussed below, may also be used to address this situation in the future.

As previously mentioned,⁵⁴ the regulation of “hybrid” embryos created by nuclear transfer will be the subject of a public consultation in the United Kingdom this year. Recent proposals dealing with potential reform to the current United Kingdom legislation on this topic have reached differing conclusions: the December 2006 white paper published by the Department of Health recommended that this practice be prohibited generally, with a mechanism in place to permit the licensing and regulation of individual experiments;⁵⁵ whereas the 2005 report of the House of Commons Science and Technology Committee suggested that this type of experiment should be permitted, with any resulting embryos being destroyed after fourteen days of development.⁵⁶

In addition to the prohibitions discussed thus far,⁵⁷ the *AHRA* also regulates several activities, including the creation of other possible animal-human combinations, as “controlled activities”.

C. Controlled Activities

No person shall, except in accordance with the regulations and a licence, combine any part or any proportion of the human genome specified in the regulations with any part of the genome of a species specified in the regulations.⁵⁸

“Human genome” in this case refers to the totality of the deoxyribonucleic acid sequence of the human species, and “species” means any taxonomic classification of non-human life.⁵⁹

The scope of this provision is impossible to determine in the absence of the regulations specifying the portions or subsets of the human genome and the species for which combinations will be restricted. Theoretically, it could cover the creation of organisms containing a haploid set of each of a human being and a non-human being,⁶⁰ the creation of transgenic animals using human genes, as well as the use of animal genes for gene therapy in humans⁶¹ (and reciprocal combinations, although these are less likely).

Existing examples of transgenic animals include the Harvard oncomouse,⁶² which was engineered with human DNA sequences to be more susceptible to cancer and to serve as a model for the human disease. Another is a “transchromosomal” mouse, whose cells contain not merely a few human genes, but an almost complete copy of human chromosome 21. Such mice are used as a model to study Down syndrome.⁶³ Many other transgenic animals are currently used in medical and pharmaceutical research as models for other diseases or for toxicity studies, or as potential donors for xenotransplantation. Transgenic animals have also been engineered to produce human proteins as drugs.⁶⁴ The creation of

⁵⁴ See HFEA Press Statement, *supra* note 4 and accompanying text.

⁵⁵ United Kingdom, Department of Health, *Review of the Human Embryology and Fertilisation Act* (London: Licensing Division, 2006) at s. 2(85).

⁵⁶ United Kingdom, House of Commons Science and Technology Committee, *Human Reproductive Technologies and the Law* (London: Stationery Office Limited, 2005) at para. 66.

⁵⁷ Subsections 5(2) and 5(3) the *AHRA* also make it an offence to offer to do or to advertise the doing of anything prohibited in subsection 5(1), and to pay or offer to pay consideration to any person for doing anything so prohibited.

⁵⁸ *AHRA*, *supra* note 8, s. 11.

⁵⁹ *Ibid.*, s. 3.

⁶⁰ The creation of these hybrids for reproductive purposes is prohibited by paragraph 5(1)(j) of the *AHRA*, but is currently not explicitly prohibited for experimental, non-reproductive purposes. Thus, regulations adopted pursuant to section 11 of the *AHRA* could be used to regulate specific types of hybrids, or methods to produce hybrids that are not currently covered by paragraph 5(1)(j).

⁶¹ As previously noted, transmissible alterations of the human genome are prohibited by the *AHRA*, so only somatic cell gene therapy would be a controlled activity.

⁶² This mouse is famous in Canada, as it was held to be a non-patentable higher life form. See *Harvard College v. Canada (Commissioner of Patents)*, 2002 SCC 76, [2002] 4 S.C.R. 45.

⁶³ Aideen O’Doherty *et al.*, “An Aneuploid Mouse Strain Carrying Human Chromosome 21 with Down Syndrome Phenotypes” (2005) 309 *Science* 2033.

⁶⁴ The first transgenically produced drug to be approved for human therapeutic use in the world is ATryn, a recombinant form of human antithrombin produced in the milk of transgenic goats. It obtained marketing approval from the European Commission on August 2, 2006, and will be used for the prevention of embolism in patients with congenital antithrombin deficiency undergoing surgery. Charlie Schmidt, “Belated approval of first recombinant protein from animal” (2006) 24:8 *Nature Biotechnology* 877. See also GTC Therapeutics, News Release, “European Commission Approves ATryn” (2 August 2006), online: GTC Therapeutics

some of these animals may be subject to section 11 of the *AHRA* in the future. In addition, because “species” as defined in this section refers to non-human life, section 11 could be used to cover other interspecies combinations involving human and plant, bacterial, yeast or viral DNA. These are currently used to produce a wide range of medications, such as insulin or growth hormone, in bioreactors. In most cases, however, regulating these combinations pursuant to a statute expressly intended to regulate human reproductive technologies might be difficult to justify.

The creation of constructs used in human gene therapy could potentially be regulated by this provision, as it often involves the combination of viral DNA and human or other genes that are introduced in human patients.⁶⁵ Although in terms of its safety and efficacy as a treatment this type of therapy would currently be regulated under the *Food and Drugs Act*,⁶⁶ any regulations adopted pursuant to the *AHRA* could impose limits on the design of these combinations. For gene therapy and most other current uses of transgenic animals, concerns like human and environmental safety are already addressed by other statutes.⁶⁷ One might therefore expect regulations aimed at preventing or licensing experiments raising “moral” questions, such as the transfer of genes participating in human cognition or speech into non-human primates, for example.

As previously mentioned, Baylis has argued that section 11 may be used to regulate the creation of “chimeras” that are not covered by paragraph 5(1)(i).⁶⁸ This argument is based upon the meaning ascribed to the word “combination”. In her opinion, mixing cells with different genomes in one organism (such as introducing animal cells in a human embryo) could be interpreted as creating a “combination” of genomes in that organism. In connection with this, it should be noted that the *Act* states that pursuant to section 11 regulations may be made “designating controlled activities or classes of controlled activities that may be authorized by a licence”,⁶⁹ and “specifying parts or proportions” of the human and other genomes to which section 11 will apply.⁷⁰ Until regulations shed more light on this, the possibility that section 11 might cover certain types of chimeras, such as the introduction of human embryonic stem cells into primate blastocysts, remains open.⁷¹

Transgenic animals, or recombinant bacteria and plants that contain sequences of non-human species but do not contain human sequences, are not addressed by this provision.

II

CHIMERAS AND HYBRIDS IN THE *AHRA* AND THE CIHR RESEARCH GUIDELINES

As previously discussed, the *AHRA* prohibits (i) the creation of chimeras that combine any cell of a non-human life form with a human embryo, while not addressing combinations involving animal embryos or human fetuses and adults, and (ii) the creation of hybrids for reproductive purposes. The focus of the *AHRA* on human embryos is understandable, given the *Act's* goal of regulating human reproductive technologies. In contrast, guidelines for federally funded research approach the topic of animal-human combinations from different angles—stem cell research and research with human subjects and human biological material. Three of the main federal granting agencies for research, including the CIHR,⁷² have jointly adopted certain research guidelines and require that these guidelines be complied with by all researchers and institutions that receive funding from them.⁷³ These include the *Stem Cell Guidelines*⁷⁴

<<http://www.transgenics.com/pressreleases/pr080206.html>> (press release issued by the manufacturer).

⁶⁵ Human Genome Project Information, “Gene Therapy”, online: Human Genome Project Information <http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genetherapy.shtml>.

⁶⁶ R.S., 1985, c. F-27.

⁶⁷ Examples are the *Food and Drugs Act*, *ibid.*, which regulates constructs used in gene therapy and drugs produced by transgenic animals, and the *Canadian Environmental Protection Act, 1999*, S.C. 1999, c. 33, which applies to the creation or introduction into Canada of new animal species.

⁶⁸ *Supra* note 46.

⁶⁹ *AHRA*, *supra* note 8, s. 65(1)(c).

⁷⁰ *Ibid.*, s. 65(1)(d).

⁷¹ Jason Scott Robert, “Regulating the Creation of Novel Beings” (2002) 11:1 Health Law Review 14 [Robert, “Regulating”].

⁷² The other agencies involved are the Social Sciences and Humanities Research Council (SSHRC) and the Natural Sciences and Engineering Research Council of Canada (NSERC), together with CIHR [Granting Agencies].

⁷³ Subsection 5(2) of the *Memorandum of Understanding* to be entered into between the Granting Agencies and an institution receiving funding requires that all such institutions receiving funding comply with both the *TCPS* and the *Stem Cell Guidelines*. See Natural Sciences and Engineering Research Council of Canada, *Memorandum of Understanding*, online: Natural Sciences and Engineering Research Council of Canada <http://www.nserc.ca/institution/mou_doc_e.htm>.

and the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*,⁷⁵ which deal with chimeras and hybrids, respectively. The *Stem Cell Guidelines* are intended to serve as an interpretation and extension of the *TCPS*, and are eventually to be integrated in the *TCPS*.

Under the *Stem Cell Guidelines*, research involving the creation of certain chimeras is not permitted: (i) research in which human or non-human embryonic stem cells, embryonic germ cells or other cells that are likely to be pluripotent are combined with a human embryo⁷⁶ or a human fetus,⁷⁷ and (ii) research in which human embryonic stem cells, embryonic germ cells, or other cells that are likely to be pluripotent are combined with a non-human embryo⁷⁸ or a non-human fetus.⁷⁹ Thus, the *Stem Cell Guidelines* not only forbid the creation of chimeras using any cells likely to be pluripotent in a human embryo, but extend the prohibition to the creation of a “chimera” at a later developmental stage (fetal) than the *AHRA*, and also to the creation of a “chimera” using non-human embryos and fetuses as a substrate for the addition of pluripotent cells of human origin. However, they do not target the use of non-pluripotent cells to create chimeras, whereas the *AHRA* prohibits the introduction of any type of animal cell into a human embryo.

As a result, in Canada, privately funded research on chimeras, being subject only to the *AHRA*, is currently less restricted than federally funded research using pluripotent cells. At the present time, experiments to create mice with human neurons by injecting pluripotent cells in mouse embryos⁸⁰ could only be carried out in Canada if neither the researcher carrying it out nor the institution of which he is a member receive funds from one of the Granting Agencies. In contrast, the National Academies of Science (United States) suggest the outright prohibition of only two types of chimeras—those in which embryonic stem cells of any origin are introduced into human blastocysts, and those created by the introduction of human pluripotent stem cells in non-human primate blastocysts.⁸¹

The narrower scope of the prohibition in the *AHRA* may reflect a concern with the constitutional validity of a wider prohibition in legislation explicitly aimed at dealing with human reproductive technologies. It is also possible that by the time the *AHRA* was enacted, research was moving in directions that seemed to make the prohibition of human-to-animal chimeras an overly restrictive measure, and regulation a preferable alternative. It bears noting that, since 1964, the *Helsinki Declaration* has explicitly required that research be carried out on animal models, where possible, prior to human experimentation.⁸²

It remains to be seen whether the federal government will adopt regulations under section 11 that aim to regulate the creation of chimeras, and what type of controls will be exerted if this occurs. As noted by Robert,⁸³ the *Proposals* initially suggested that the creation of chimeras be a regulated activity, and

⁷⁴ *Supra* note 47.

⁷⁵ Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council, and Social Sciences and Humanities Research Council, *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (1998, with 2000, 2002, and 2005 amendments), online: Interagency Advisory Panel on Research Ethics <http://www.pre.ethics.gc.ca/english/pdf/TCPS%20October%202005_E.pdf> [TCPS].

⁷⁶ *Stem Cell Guidelines*, *supra* note 47, s. 8(2)(4).

⁷⁷ *Ibid.*, s. 8(2)(5).

⁷⁸ *Ibid.*, s. 8(2)(6).

⁷⁹ *Ibid.*, s. 8(2)(7).

⁸⁰ See e.g. Muotri *et al.*, *supra* note 45.

⁸¹ National Research Council, National Academy of Sciences, Committee on Guidelines for Human Embryonic Stem Cell Research, *Guidelines for Human Embryonic Stem Cell Research* (Washington, D.C.: National Academies Press, 2005) recommendation 3(c) [American Guidelines]. However, research involving the introduction of human embryonic stem cells into non-human animals at any stage of development is singled out for review by an ESCRO committee in addition to the usual animal use committees and institutional review board reviews. See also recommendation 3(b).

⁸² World Medical Association, *World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*, adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and amended by the 29th WMA General Assembly, Tokyo, Japan, October 1975, 35th WMA General Assembly, Venice, Italy, October 1983, 41st WMA General Assembly, Hong Kong, September 1989, 48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996 and the 52nd WMA General Assembly, Edinburgh, Scotland, October 2000, note of clarification on Paragraph 29 added by the WMA General Assembly, Washington 2002, and note of clarification on Paragraph 30 added by the WMA General Assembly, Tokyo 2004 [*Helsinki Declaration*], online: World Medical Association <<http://www.wma.net/e/policy/pdf/17c.pdf>>. See article 11, which states:

Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

⁸³ Robert, “Regulating”, *supra* note 71.

contained a much broader definition of “chimera” than does the *Act*;⁸⁴ this definition included animal-to-human chimeras created at the fetal stage, as well as human-to-animal chimeras created at both the embryonic and fetal stages. Thus, the previously expressed intention to regulate some types of chimeras not currently prohibited may resurface.

In the case of hybrids, a difference between the statutory provisions of the *AHRA* and the federal guidelines also exists. The *TCPS* deems it unacceptable to create or intend to create hybrid individuals,⁸⁵ or to undertake research that involves the *formation* of animal-human hybrids.⁸⁶ These prohibitions seem to target the creation of hybrids for both research and reproductive purposes, in contrast to the *Act*. The *TCPS* would appear to prohibit the transfer of human nuclei into, for example, the rabbit oocytes previously described, although it does not define “hybrid”, so it is difficult to ascertain whether it intended to cover hybrids resulting from nuclear transfer experiments. Thus, hybrids present another case in which experiments in privately funded institutions currently seem to be less restricted than federally funded research. As with chimera regulation, it may be that the creation of hybrids for research will be further regulated pursuant to section 11 of the *AHRA*.

III

ENFORCEMENT: OFFENCES AND GRANDFATHERING CLAUSE

The consent of the Attorney General of Canada must be obtained before prosecution for an offence under the *AHRA*.⁸⁷ Breaches of the regulatory schemes set up by the *Act* have serious consequences. The prohibitions against animal-human combinations are given “teeth” by section 60 of the *AHRA*, which makes it an offence to contravene any of them. Conviction on indictment can entail a fine not exceeding \$500,000, imprisonment for a term not exceeding ten years, or both, while a summary conviction means liability for a fine up to \$250,000, imprisonment for a period not exceeding four years, or both.

For controlled activities like those eventually targeted by section 11, the picture is different. Section 71 reads as follows:

Notwithstanding sections 10 to 13, a person who undertakes a controlled activity at least once during the period of one year preceding the coming into force of those sections may subsequently, without a licence, undertake the controlled activity and use any premises required for that purpose until a day fixed by the regulations.⁸⁸

Thus, technically, since section 11 came into force on April 22, 2004, anyone who was performing the type of experiment referred to in section 11 may continue to do so until regulations fix a date when the licence will become necessary. The difficulty is that, while section 11 is technically in force, the absence of the regulations referred to in this provision renders it impossible to determine which activities require a licence, and therefore which activities may only be carried out by persons who were carrying them out before April 22, 2004. This seems to rob the transitory measure of section 71 of any effect in connection with section 11. Thus, effectively, experiments that involve combining the human genome with portions of the genome of other species may currently be undertaken by anyone (to the extent they are not prohibited by other legislative provisions). Once the regulations are adopted, and unless they provide otherwise, a literal interpretation of section 71 would be to “grandfather” those whose activities before April 22, 2004 were covered by section 11 but not those who have begun similar activities after that date.

A person convicted of a breach of the regulations, or of the sections requiring a licence for “controlled activities”, such as section 11 of the *AHRA*, is liable, on conviction or indictment, to a fine of up to \$250,000 or imprisonment for a term not exceeding five years, or both. On summary conviction this

⁸⁴ See *Proposals*, *supra* note 13, s. 9(3).

⁸⁵ See *TCPS*, *supra* note 75, art. 9(3), which reads as follows:
It is not ethically acceptable to create, or intend to create, hybrid individuals by such means as mixing human and animal gametes, or transferring somatic or germ cell nuclei between cells of humans and other species.

⁸⁶ *Ibid.*, art. 9.5, which reads as follows:
It is not ethically acceptable to undertake research that involves ectogenesis, cloning human beings by any means including somatic cell nuclear transfer, formation of animal/human hybrids, or the transfer of embryos between humans and other species.

⁸⁷ *AHRA*, *supra* note 8, s. 63.

⁸⁸ This provision seems to have a “freezing” effect. Persons who manipulate human reproductive material for the purpose of creating an embryo, for example, an activity regulated pursuant to section 10 of the *AHRA*, may continue to do so if they were performing these activities prior to April 22, 2004, the date section 10 came into force, until the regulations fix a date when a licence will be required. Until the Agency becomes operational and the regulations concerning licences are adopted, therefore, no one who was not carrying out these activities before may begin to do so.

person would be liable to a fine not exceeding \$100,000, imprisonment for a term not exceeding two years, or both.⁸⁹

In addition, a court imposing a fine or term of imprisonment in respect of an offence under the *AHRA* may order the forfeiture and disposition of any material or information by means of which, or in relation to which, the offence was committed. If such an order is applied for by the attorney general, moreover, a court may order the convicted person not to engage in any activity that in its opinion may lead to the commission of an offence under the *AHRA*.⁹⁰

The Agency may also notify professional licensing or disciplinary bodies of the identity of persons charged with an offence under the *AHRA*, or for whom there are reasonable grounds to believe that they acted in breach of a professional code of conduct.⁹¹

IV CONSTITUTIONAL NOTE

The constitutionality of the *AHRA* has been the subject of some comment,⁹² with several authors arguing that the recourse to regulatory schemes creating criminal offences was necessary to anchor the legislation within federal jurisdiction. Although any detailed analysis of this topic is beyond the scope of this article, some remarks are necessary because the constitutionality of the *Act* bears on the regulation of animal-human combinations in Canada. Most authors agree that the constitutional basis for the federal government's passage of the *AHRA* is its exclusive authority to legislate for criminal law.⁹³ However, general jurisdiction over health matters, such as the provision of health care, is usually understood to be with the provincial domain.⁹⁴ Assisted human reproduction services, such as *in vitro* fertilization, are generally characterized as health services, which presents the possibility that provinces may claim that they properly fall within their jurisdiction. For this reason, certain provisions of the *AHRA* dealing with controlled activities are open to constitutional challenge.⁹⁵

Perhaps in recognition of this, the *AHRA* itself provides that certain of its provisions—describing controlled activities, aspects of privacy of personal information, and enforcement,⁹⁶ and corresponding regulations—may not apply in a province if the federal minister of health and the government of that province agree in writing that there are laws in force in the province that are equivalent to the *AHRA* provisions.⁹⁷ This could be understood as a mechanism to foster cooperation between the different levels of government in order to achieve uniform regulation without triggering a jurisdictional debate.

The Government of Quebec is of the opinion that the *AHRA* exceeds the federal government's jurisdiction by legislating in the area of health and civil rights. As a result, the Attorney General of Quebec has been mandated by order in council to proceed with a reference case before the Quebec Court of Appeal, questioning whether the federal government has overstepped its jurisdiction by adopting sections

⁸⁹ *AHRA*, *supra* note 8, s. 61.

⁹⁰ *Ibid.*, s. 63.

⁹¹ *Ibid.*, s. 64.

⁹² See Rivard & Hunter, *supra* note 36, at 28–30. See also, *inter alia*, the following articles: Alison Harvison-Young & Angela Wasunna, "Wrestling with the Limits of Law: Regulating New Reproductive Technologies" (1998) 6 Health L.J. 239 at 255 (concerning a previous draft bill on assisted reproductive technologies); National Health Law and Family Law Sections, Canadian Bar Association, "Submission on Draft Legislation on Assisted Human Reproduction" (2002) 10:2 Health Law Review 25; Angela Campbell, "A Place for Criminal Law in the Regulation of Reproductive Technologies" (2002) 10 Health L.J. 77 at 95; Alison Harvison-Young, "Let's Try Again... This Time with Feeling: Bill C-6 and New Reproductive Technologies" (2005) 38 U.B.C. L. Rev. 123 [Harvison-Young, "Let's Try Again"].

⁹³ *Constitution Act, 1867* (U.K.), 30 & 31 Vict., c. 3, s. 91(27), reprinted in R.S.C. 1985, App. II, No. 5 [*Constitution Act, 1867*]. The federal government also has authority to legislate for the peace, order and good government of the country, but this power has seen variation in its interpretation in recent years and is not seen as secure a basis for legislation dealing with services, such as *in vitro* fertilization, that are perceived as health services. See Harvison-Young, "Let's Try Again", *ibid.*, for a discussion of this.

⁹⁴ This is based on those provisions of the *Constitution Act, 1867*, *ibid.*, granting jurisdiction to the provinces for the "Establishment, Maintenance, and Management of Hospitals, Asylums, Charities, and Eleemosynary Institutions in and for the Province, other than Marine Hospitals" (s. 92(7)), "Property and Civil Rights in the Province" (s. 92(13)), and "Generally all Matters of a merely local or private Nature in the Province" (s. 92(16)).

⁹⁵ Besides the provisions explored in this paper concerning animal-human combinations, the *AHRA* aims to prohibit or regulate the use of reproductive material without consent, use of human reproductive material, including for the provision of infertility services, protection of minors, and expense reimbursement for surrogate mothers.

⁹⁶ *AHRA*, *supra* note 8, ss. 10–16, 46–53, 61.

⁹⁷ *Ibid.*, s. 68.

8–12 of the *AHRA*.⁹⁸ This challenge is not concerned with the criminal prohibitions against animal-human combinations contained in section 5 of the *AHRA*, but it does target section 11, which purports to regulate the combination of the human genome with that of other species. As previously mentioned, this section is, in practice, currently inoperative because the regulations that would give it effect have not been adopted. As a result, Quebec's constitutional challenge of the *AHRA*, even if successful, would not have any immediate effect on the regulation of animal-human combinations as it now exists. However, if section 11 is found to lie outside the competence of the federal government, Quebec's challenge may succeed in preventing federal regulation of animal-human combinations at the genome or genetic level pursuant to section 11 the *AHRA* in the whole of Canada. This would not be conducive to the "one standard" approach that is often perceived as desirable in these matters, but would respect the autonomy of the provinces on matters within their jurisdiction. Eventually, if the provinces adopted different regimes for these animal-human combinations, and in the absence of professional self-regulation, researchers might resort to "forum-shopping" within the country for such experiments. It should be kept in mind, however, that research conducted under the auspices of federal granting agencies would still be subject to the *Stem Cell Guidelines*, the *TCPS*, or other such government policies.

On December 16, 2004, the Government of Quebec tabled Bill 89, *An Act respecting clinical and research activities as regards assisted human reproduction and amending other legislative provisions*, which deals with assisted human reproduction activities but does not address the question of animal-human combinations.⁹⁹ At the time of the writing of this article this bill has not been passed. If enacted and judged equivalent to the *AHRA* by the federal and provincial governments through a reciprocity agreement, the Quebec *Act* would apply in Quebec. Bill 89 does not contain a provision equivalent to section 11 of the *AHRA* or one dealing explicitly with animal-human combinations at the genome level. It is therefore unlikely that section 11 would be included in such a reciprocity agreement unless the current text of the bill is amended.

V

ETHICAL CONSIDERATIONS UNDERLYING THE REGULATION OF ANIMAL-HUMAN COMBINATIONS IN THE *AHRA*

The *AHRA* opens with a declaration of the interpretive principles that apply to it.¹⁰⁰ In the context of animal-human combinations, the most relevant principles cited are "the protection and promotion of human health, safety, dignity and rights" in the use of assisted human reproductive technologies and related research,¹⁰¹ as well as the protection of "human individuality and diversity" and of "the integrity of the human genome".¹⁰² Before a conclusion is reached as to the scope of the *AHRA* and its likely effect in the field of animal-human combinations, these interpretive principles will be very briefly reviewed¹⁰³ in order to determine the extent to which they might underlie the prohibitions¹⁰⁴ set forth in the *AHRA*.

A. Health and Safety

The protection and promotion of human health and safety are explicitly identified in the *AHRA* as key concerns. The Standing Committee on Health, when reporting on a draft version of the *AHRA*, was concerned with the safety of both the transplantation of animal reproductive material into a human, and

⁹⁸ D. 1177-2004, G.O.Q. 2005.II.62 (Order in council 1177-2004, December 15, 2004). The reference to the Quebec Court of Appeal has been scheduled for hearing on September 19, 2007. A constitutional challenge was also initiated by the Quebec government in respect of the federal privacy and information statute, the *Personal Information Protection and Electronic Documents Act*, S.C. 2000, c. 5, which provides that the Canadian privacy commissioner may declare that a province has equivalent privacy legislation in place, in which case the federal act will not apply in that province except to federal undertakings. See D. 1368-2003, G.O.Q. 2004.II.184. The reference to the Quebec Court of Appeal on this is not yet scheduled for a hearing.

⁹⁹ 1st Sess., 37th Leg., 2004.

¹⁰⁰ *AHRA*, *supra* note 8, s. 2.

¹⁰¹ *Ibid.*, s. 2(b). Section 22 of the *AHRA* also states that the objectives of the Agency (when functioning) will be to protect and promote the health and safety, and the human dignity and human rights, of Canadians, as well as to foster the application of ethical principles in relation to assisted human reproduction and other matters to which the *AHRA* applies, including research.

¹⁰² *Ibid.*, s. 2(g).

¹⁰³ An in-depth consideration of these topics is beyond the scope of this paper.

¹⁰⁴ Because no regulations have been passed to permit us to ascertain the scope of section 11, meaningful discussion of this section is not possible at this time.

the reverse. As a matter of consistency, it also recommended that the creation of animal-hybrids for reproductive purposes be banned.¹⁰⁵

In the context of animal-human combinations, safety concerns include the possibility that new human diseases might arise from the close proximity of animal and human tissue through “humanization” of animal pathogens.¹⁰⁶ Recent examples of the “humanization” of an animal pathogen causing new human diseases are SARS¹⁰⁷ and mutations of an avian flu virus that have been shown to be transmissible among humans, with serious consequences.¹⁰⁸ This would be a concern in all cases of the transfer of biological material between humans and animals, or of animal-human combinations prohibited by the *AHRA*. It is also a serious concern in xenotransplantation¹⁰⁹ and other types of animal-human combinations that the *AHRA* does not cover. As a serious risk that is not well understood, the possibility of zoonoses requires careful consideration of safety measures for all situations in which biological materials of animal origin are put in close contact with human beings.

The prevention of zoonoses alone, however, does not explain the prohibitions found in the *AHRA*. Whereas the creation of chimeras by adding material of human origin to a human embryo is prohibited, the creation of similar chimeras at the fetal stage is not. Similarly, the converse experiment of adding material of human origin to an animal embryo or fetus is not prohibited, despite the fact that it raises questions with respect to pathogens.¹¹⁰ Thus, the possible humanization of animal pathogens does not by itself explain the structure of the regulatory scheme.

Another health and safety concern is the possibility of creating beings suffering from serious malformations and disorders. To a certain extent, the prohibitions of the *AHRA* seem to take this danger into account. For example, no hybrid being may be created for reproductive purposes, because the results of the interaction between two different haploid genomes are unknown. Similarly, animal-to-human chimeras constructed at the embryonic level, where the introduction of foreign material might have the greatest effect on development of the organism, are prohibited. However, this possibility does not fully account for the chosen regime: although from a developmental point of view an organism at the embryonic stage is most vulnerable to the introduction of “foreign” biological material, a fetus is probably also quite vulnerable to such a manipulation, which might cause malformation or disease. Furthermore, the introduction of human material in a non-human embryo is not prohibited under the *AHRA*. A suffering, malformed being could certainly arise from this type of experiment. It must be concluded that these concerns, although real, lie outside the appropriate scope of the *AHRA*, and should therefore be left to other statutes or regimes dealing with the protection of human beings in medicine and research, or the protection of animals used in research.

The regulations eventually adopted under section 11 may alter this analysis, because they could effectively create additional prohibitions. It remains that decisions based on safety are not sufficient to explain the *a priori* choice of prohibitions made in the *AHRA*. The focus of the *AHRA* on human reproduction may explain it in part, but documents prepared in connection with the legislative process suggest that other factors are also involved.

B. Human Dignity

The protection and promotion of human dignity and human rights are explicitly referred to in section 2 of the *AHRA* as principles that must guide its application, but the *Act* itself does not provide any further interpretive insight. The *AHRA* was based on the work carried out by the Royal Commission, which recommended that human zygote/embryo research related to animal-human hybrids and the transfer of zygotes to another species be prohibited under threat of criminal sanction.¹¹¹ The Commission grounded its recommendations on an exploration of the attitudes of Canadians and on its own ethical reasoning. Its

¹⁰⁵ Standing Committee Report, *supra* note 14.

¹⁰⁶ Such diseases are referred to as “zoonoses”.

¹⁰⁷ Wendong Li *et al.*, “Bats Are Natural Reservoirs of SARS-Like Coronaviruses” (2005) 310 *Science* 676; Dennis Normile, “Researchers Tie Deadly SARS Virus to Bats” (2005) 309 *Science* 2154.

¹⁰⁸ Declan Butler, “Family Tragedy Spotlights Flu Mutations” (2006) 442 *Nature* 114.

¹⁰⁹ See Health Canada, *Proposed Canadian Standard for Xenotransplantation, Draft 14*, available upon request from Health Canada.

¹¹⁰ These animals are generally isolated from the outside world in a way that human beings cannot be, so the potential risk in this case may be smaller.

¹¹¹ Commission Report, *supra* note 10 at 637.

report notes that certain manipulations, such as interspecies crosses, are unethical in themselves when applied to human beings, and contrary to the Commission's ethical principles and the values of Canadians.¹¹² The creation of an animal-human hybrid would deny the embryo's connection to the human community, and thus violates human dignity.¹¹³

The House of Commons Standing Committee on Health commented that both the transplantation of animal reproductive material into a human¹¹⁴ and the use of human reproductive material or an *in vitro* embryo that was transplanted into a non-human life form for reproductive purposes¹¹⁵ contravene human dignity, without providing further explanation.

The perception that animal-human combinations offend human dignity seems central to the legislative choices made in the *AHRA*, but very little is in fact offered to support this viewpoint. In the bioethics literature the concept of human dignity remains an elusive one, readily invoked (especially in the field of biotechnology) but without a common meaning and often without adequate explanation concerning how and why it is infringed.¹¹⁶ A common justification for attributing dignity to human beings is that, because they share certain characteristics, they should be treated as ends in themselves.¹¹⁷ Basing dignity on the possession of these characteristics, of course, begs the question of what to do with human beings that do not possess them, or beings other than humans who do. These questions are far from resolved.

In international instruments, all born members of the human species have human dignity, which grounds their enjoyment of human rights.¹¹⁸ According to article 1 of the *Universal Declaration on the Human Genome and Human Rights*,¹¹⁹ the human genome at the level of the species is what grounds the recognition of humanity and of an individual being's dignity. Thus, some international instruments display a "species-centric" approach to human dignity.

The prohibitions in the *AHRA* appear to cluster around the exchange or combination of reproductive material or very early developmental material between species. They focus on cases in which the animal-human combination may affect the apparent "human" character of the resulting being, making it no longer wholly human. This tends to support a "species-centric" view of dignity.

If that is the underlying logic of the *AHRA*, the prohibition against creating chimeras at the embryonic, but not the fetal or later, stage may seem like an omission. It may be that a fetus—defined in the *AHRA* as the human being from the fifty-seventh day of development—is already sufficiently developed that its "human" character would not be affected by the combination. However, manipulation at this stage could still have profound effects on the developing organism. It may also be that a fetus affected with a disease could benefit from cell therapy, and that this possibility would make chimeras at the fetal stage a matter for regulation rather than prohibition. That this avenue is left open (although it may be regulated at a later date) suggests that the possibility of therapy may be a better example of

¹¹² *Ibid.* According to the Commission, there is widespread agreement among Canadians that the formation of animal-human hybrids and the gestation of human zygotes in the uterus of another species are unacceptable.

¹¹³ See *ibid.* at 55 for a brief discussion of the Commission's view on human dignity.

¹¹⁴ Standing Committee Report, *supra* note 14.

¹¹⁵ *Ibid.*

¹¹⁶ Timothy Caulfield & Roger Brownsword, "Human dignity: a guide to policy making in the biotechnology era?" (2006) 7:1 *Nature Reviews Genetics* 72. See also Jason Scott Robert, "The science and ethics of making part-human animals in stem cell biology" (2006) 20:7 *Federation of American Societies for Experimental Biology Journal* 838 [Robert, "Science and Ethics"].

¹¹⁷ The question of which characteristics confer dignity on human beings (and whether any number of them is necessary or sufficient for this) is a controversial one and will not be dealt with here in any detail. It has been argued, in the context of discussions on chimeras, that the capacities required for human dignity include not only the ability to reason, choose freely, and act for moral reasons, but also the ability to use a sophisticated language, function in a complex social network, develop a worldview, and display empathy and sympathy, for example. Philip Karpowicz, Cynthia B. Cohen & Derek van der Kooy, "Developing Human-Nonhuman Chimeras in Human Stem Cell Research: Ethical Issues and Boundaries" (2005) 15:2 *Kennedy Institute of Ethics Journal* 107 [Karpowicz, Cohen & van der Kooy].

¹¹⁸ See *Universal Declaration of Human Rights*, GA Res. 217(III), UN GAOR, 3d Sess., Supp. No. 13, UN Doc. A/810 (1948) 71, [UDHR] art. 1, which states: "All human beings are born free and equal in dignity and rights." It is interesting in connection with this to note that the *Canadian Charter of Rights and Freedoms*, Part I of the *Constitution Act, 1982*, being Schedule B to the *Canada Act 1982* (U.K.), 1982, c. 11, and the *Canadian Human Rights Act*, R.S.C. 2985, c. H-6, do not mention dignity at all, while the *Canadian Bill of Rights*, S.C. 1960, c. 44 mentions it in its preamble. In contrast, all the provincial and territorial human rights legislation refers to human dignity, some referring to the *UDHR*.

¹¹⁹ GC Res. 29 C/16, UNESCO(OR), 29 Sess., (1997), GA Res. 152, U.N. GAOR, 53d Sess., U.N. Doc. A/RES/53/152 (1999) [1997 Declaration].

respect for human dignity than the preservation of the “pure” human character of the developing human being.

It is interesting in this respect to note that although chimeras (in the *AHRA*, the combination of cells of animal or human origin with a human embryo) may not be produced at all, hybrids may not be produced for *reproductive purposes*. The human embryo is granted a status that does not permit it to be mixed with “other” biological material at all. On the other hand, the human “embryo” that would result from cross-species fertilization can apparently be created and then destroyed for research purposes. This also supports the idea that a “species-centric” view of human dignity underlies some of the prohibitions included in the *Act*, and raises anew the question of the status of an “embryo” created by introducing a human nucleus in a non-human egg. As a “hybrid” under the *AHRA*, this embryo may not be created for reproductive purposes, but could be created for experimental purposes (unless regulations provide otherwise in the future). As previously discussed, this embryo would be genetically mostly human,¹²⁰ yet it seems to be treated differently.¹²¹

The regulations adopted pursuant to the *AHRA*, when known, may allow us to draw better conclusions about the conception of human dignity underlying the current regulatory scheme for animal-human combinations.¹²² How the creation of a chimera using an animal embryo and human cells will be treated, for example, could be revealing. Concerns have been expressed that this type of manipulation could result in a being with “almost-human” attributes,¹²³ such as increased cognitive ability.¹²⁴ From the perspective that bases human dignity on the possession of a cluster of capacities, this creates concern: some feel that creating a chimera using an animal embryo and human cells violates human dignity, because the human capacities tied to dignity would be transferred to an organism unable to fully exercise them due to physical limitations.¹²⁵ Others are afraid of our probable failure to treat such a creature appropriately.¹²⁶ Interestingly, both viewpoints approve of the prohibition of experiments involving the transfer of human pluripotent cells into non-human primate blastocysts found in the American Guidelines.¹²⁷ The Canadian *Stem Cell Guidelines* currently take a more restrictive stance, prohibiting this type of experiment for all animal embryos and fetuses.¹²⁸

This brief exploration of human dignity as a basis for the regulation of animal-human combinations confirms a recent observation: in a pluralistic society “human dignity”, although an ill-defined concept, can justify prohibitions on biotechnology because of its “constructive ambiguity”.¹²⁹ Despite this, a better articulation of the reasons why certain animal-human combinations are seen as violations of human dignity is clearly required.¹³⁰

¹²⁰ See *supra* note 53.

¹²¹ This difference in treatment may be due to an assumption that this “embryo” cannot develop and is not therefore a potential human life; however, that assumption cannot be fully tested without contravening the *Act*, since hybrids cannot be created for “reproductive purposes”. Some insight may be gained into this question by allowing *in vitro* development of these embryos for a length of time. No legislative or regulatory provisions currently govern the time periods during which such embryos might be kept *in vitro*.

¹²² Although at first blush experiments involving animals and human cells, or animal and human genes, may seem to lie outside the scope of the *AHRA*, the definition of “human reproductive material” includes human cells and genes, which would allow these types of experiments to be classified as research-related to assisted human reproduction. It is by no means certain, however, that regulations concerning additional chimeras will in fact be adopted under the *AHRA*.

¹²³ This possibility is taken seriously by some legal scholars, who have discussed the granting of personhood to certain kinds of chimeric or transgenic animals: D. Scott Bennett, “Comment: Chimera and the Continuum of Humanity: Erasing the Line of Constitutional Personhood” (2006) 55 *Emory L.J.* 347; Michael D. Rivard, “Comment: Toward a General Theory of Constitutional Personhood: A Theory of Constitutional Personhood for Transgenic Humanoid Species” (1992) 39 *UCLA L. Rev.* 1425.

¹²⁴ A similar concern may apply to transgenic animals—assuming that genes involved in human cognition were identified and transferred to close relatives of human beings such as chimpanzee, for example. These types of experiments may be what will be targeted by regulation under section 11.

¹²⁵ Karpowicz, Cohen & van der Kooy, *supra* note 117.

¹²⁶ From this perspective, the creation of such “enhanced” animals is not an infringement of human or animal dignity, so long as the resulting being is treated appropriately, given its moral status. Robert Steiffer, “At the Edge of Humanity: Human Stem Cells, Chimeras, and Moral Status” (2005) 15:4 *Kennedy Institute of Ethics Journal* 347 [Steiffer].

¹²⁷ *Supra* note 81.

¹²⁸ *Supra* note 47, ss. 8(2)(4)–8(2)(7).

¹²⁹ Caulfield & Brownsword, *supra* note 116.

¹³⁰ *Ibid.*; Robert, “Science and Ethics”, *supra* note 116; Steiffer, *supra* note 126.

C. Individuality

Intertwined with human dignity is the notion of individuality, which also seems to play a role in explaining the prohibitions on chimeras found in the *AHRA*. In the creation of a “chimera”¹³¹ cells from a different organism are added to an existing embryo. This embryo already contains all of the genetic instructions necessary to make a human being, if the appropriate environment is provided. The introduction of foreign material from an animal may markedly affect its development and characteristics. The *AHRA* prohibitions can therefore be understood as expressing a concern for preserving the individuality of the future person.

Although the manipulation of a human embryo in this manner most likely involves considerations of human dignity, the prohibition on human-human and animal-human chimeras implies that some notion in addition to that of human dignity is involved. The objection must be not only to the introduction of animal material, but of material that, even if from a human being, will seriously affect the development of the existing embryo and compromise its identity and individuality.

Human individuality and identity are also concerns identified in international instruments, although they are ordinarily mentioned to underline the contribution of factors other than genetics to individuality¹³² and to prohibit discrimination against persons on the basis of their genetic identity.¹³³ They are not discussed in the context of animal-human combinations.¹³⁴

D. Protection of the Human Genome

In addition to more general issues of human dignity and individuality, a concern for the integrity of the human genome underlies the prohibition of certain animal-human combinations. Each individual human being is the embodiment of its expressed genome, giving the genome a personal dimension that places it within the scope of individual autonomy. However, an individual’s genome also has a connection with that of others, because it is transmitted to a person’s descendants. Therefore, any changes made by the individual to the personal genome will affect others.

The *AHRA* explicitly prohibits the intentional alteration of the human genome, whether in a human being or an embryo, such that the alteration is capable of being transmitted to descendants.¹³⁵ The combination of the human genome with portions of the genome of another species, whether directly (as in making a hybrid or transgenic being) or indirectly (as a result of cell fusion in a chimeric creature¹³⁶) also raises the question of possibly transmissible alterations in the human genome.

¹³¹ As defined in the *AHRA*, *supra* note 8, s. 3.

¹³² See article 3 of the *International Declaration on Human Genetic Data*, GC Res. 22 UNESCO(OR), 31st Sess., (2003), which reads as follows:

Each individual has a characteristic genetic make-up. Nevertheless, a person’s identity should not be reduced to genetic characteristics, since it involves complex educational, environmental and personal factors and emotional, social, spiritual and cultural bonds with others and implies a dimension of freedom.

See also the preamble to the *Universal Declaration on Bioethics and Human Rights*, GC Res. 36 UNESCO(OR) 33d Sess., (2005) [2005 Declaration], which states that “a person’s identity includes biological, psychological, social, cultural and spiritual dimensions”.

¹³³ See article 2 of the 1997 Declaration, *supra* note 119, which reads as follows:

(a) Everyone has a right to respect for their dignity and for their rights regardless of their genetic characteristics.
(b) That dignity makes it imperative not to reduce individuals to their genetic characteristics and to respect their uniqueness and diversity.

See also article 1 of the Council of Europe, P.A., *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine* (4 April 1997, Eur. T.S. 164, entry in force December 1, 1999) [Oviedo Convention], which states in its relevant part:

Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.

¹³⁴ The *Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings* (12 January 1998, Eur. T. S. 168, entry in force March 1, 2001) seems to consider that cloning, being the process of creating a human being with the same nuclear gene set as another human being, is a threat to the identity of human beings.

¹³⁵ For a discussion of the dignity debate in the context of transmissible mutations of the human genome, see Law Reform Commission of Canada, *Human Dignity and Genetic Heritage: a study paper* by Bartha Maria Knoppers (Ottawa: Law Reform Commission of Canada, 1991) [Knoppers]; see also Caulfield & Brownsword, *supra* note 116.

¹³⁶ It could also be queried whether, even if there is no cell fusion and therefore no contact between the two genomes involved in a chimera *in the same cell*, the co-expression of two genomes in the same organism could be seen as threatening the integrity of each of them individually.

One strong argument for avoiding transmissible changes in the human genome is that we currently lack scientific knowledge of the effect of such changes on the gene pool and on the general fitness of the species. Complex gene-environment interactions make this kind of prediction extremely difficult, even in the case of attempting to “correct” apparently deleterious mutations.¹³⁷ This uncertainty may apply all the more to modifications that mix animal and human sequences.

Other reasons for specifically protecting the human genome have been expanded upon in international instruments. Unfortunately, these instruments do not deal explicitly with animal-human combinations. As previously mentioned, according to article 1 of the 1997 Declaration, the human genome is what grounds the recognition of humanity and of an individual being’s dignity. In addition, as the “heritage of humanity”, the human genome (at the level of the species) must be protected as a common resource for future generations.¹³⁸ Thus, the modification of one’s genome in a transmissible manner seems to exceed the scope of purely individual autonomy and may even threaten the dignity of future humans.

Taken together, these considerations would point towards restricting experiments that might generate beings with a modified, but recognizably human, genome,¹³⁹ or at least require that their reproduction be prohibited, a recommendation found in the American Guidelines.¹⁴⁰

CONCLUSION

This paper has reviewed certain aspects of animal-human combinations in Canada, as regulated by the *Assisted Human Reproduction Act*. Although not entirely in force, the *Act* prohibits the use of non-human reproductive material in humans, the use in humans of human reproductive material previously transplanted into a non-human life form, the creation of chimeras by adding material of non-human origin to human embryos, and the creation for reproductive purposes of human/non-human hybrids. In the future, the creation of some transgenic life forms may also be regulated pursuant to section 11 of the *Act*.

The creation of certain types of animal-human chimeras, such as those obtained by introducing cells of animal origin into a human fetus, and introducing material of non-human or human origin into a non-human embryo, are not currently prohibited activities under the *Act*. The creation of hybrids (including by nuclear transfer) for non-reproductive purposes also appears to be permitted. These activities may eventually be regulated, although no draft regulations concerning animal-human combinations have yet been published. In the meantime, certain differences subsist in Canada between what is permissible for researchers and institutions funded by federal agencies, currently restricted from carrying out certain experiments, and in privately funded research.

Overall, the *Act* seems calibrated to prohibit the creation of animal-human combinations that are currently unsafe, as well as scientifically and ethically problematic, while leaving open the possibility of regulating other such combinations with more immediate scientific potential, although these also raise ethical questions. Despite not being mentioned in the *Act*, freedom of research seems to have been an important consideration underlying this scheme. A recognition that benefits flow from research is found in subsection 2(b), which states that the protection and promotion of human health, safety, dignity, and rights is the best way to secure the benefits of research related to assisted human reproductive technologies for individuals and society. Thus, freedom of research must be exercised in a way that takes ethical considerations into account, and experiments must be scientifically valid and ethically justifiable.¹⁴¹ The development of the regulatory framework under the *Act* will reveal how these various concerns will be balanced against each other.

¹³⁷ One example of this is the selective advantage apparently conferred on carriers of the sickle cell disease trait against malaria mortality, despite the high mortality rate among homozygotes. See Michael Aidoo *et al.*, “Protective effects of the sickle cell gene against malaria morbidity and mortality” (2002) 359 *Lancet* 1311.

¹³⁸ This concern is also present in the 2005 Declaration, *supra* note 132, which states at article 16 that “the impact of life sciences on future generations, including on their genetic constitution, should be given due regard”, and in the *Oviedo Convention*, *supra* note 133, article 13 of which permits only preventive, diagnostic, or therapeutic interventions on the genome, that do not aim to introduce changes in the genome of descendants. For a critique of this “naturalist” or static approach, see Knoppers, *supra* note 135.

¹³⁹ The question of what is a “human genome” is of course raised here; much like the question of what is a “human being”, it is a difficult question that reaches well beyond the scope of this paper.

¹⁴⁰ American Guidelines, *supra* note 81, recommendation 3(c)(iii).

¹⁴¹ This is discussed in the context of chimeras in Robert, “Science and Ethics”, *supra* note 116.